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To: Dr. T. S. Osdene Date: November 5, 1981

From: E. B. Sanders

Subject: 1982 Plans and Objectives - Chemical Research Division

The objectives for the Chemical Research Divison during 1982 are as follows:

A. Precursor-Product Studies

The majority of the effort in this area will be devoted to a thorough study of the contribution of nicotine to the formation of aza-arenes. Less extensive studies will be directed towards 1) an attempt to determine the nitrogenous precursor(s) of the nitroso group in volatile nitrosamines; 2) the smoke chemistry of rutin; and 3) the determination of the contribution of the various blend components to mainstream smoke of low and ultra-low delivery cigarettes. All of these projects will utilize labelled precursors and all, except for the last study, will attempt to identify precursors which lead to undesirable products with the hope of ultimately learning to eliminate such products thereby leading to improved products. The last study represents a rational approach to blending in low delivery cigarettes.

A very different type of precursor-product study is represented by our proposed work with Amadori compounds. We anticipate that a detailed study of the products formed from the thermalization of a number of these compounds (via either pyrolysis or on smoking) may lead to an improvement of the cooked flavor system.

B. Isolation and/or Synthesis of Labelled Compounds

This work will be carried out to provide labelled compounds necessary for both precursor-product and filter efficiency studies. Compounds to be made include ^{14}C-nicotine, ^{14}C-alkylpyrazines, ^{14}C-menthol, ^{14}C-rutin, and $^{15}NO_3^-$ and $^{15}NO_2^-$.

C. Investigations of Thermal Mechanisms

The ultimate goal of precursor-product studies

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is to identify the precursors of either undesirable or desirable products and then to control their formation. Although considerable work has been done in the past involving the "identify" portion of these studies, little has been done with regard to "control." As a consequence we plan to initiate a detailed study of the reaction of nitrite (assuming that we first experimentally confirm nitrite as a direct precursor of volatile nitrosamines in a cigarette) with secondary amines as a function of several reaction variables such as temperature, pH, etc. Based on the results of these studies we would hope to be able to rationally modify the chemistry taking place in a cigarette to reduce the formation of volatile nitrosamines.

D. Transfer of Inorganics to Smoke

These studies will continue with most of the emphasis being placed on the transfer of calcium utilizing ^{45}Ca labelled tobacco. Calcium transfer to smoke has previously been shown to be atypical, and it is hoped to discover the causes of this anomolous behavior.

E. Low Level Laboratory

Construction of the low level laboratory should be completed in 1982. Initial work projected will be environmental monitoring of tobacco and tobacco by-products.

F. Development of New Instrumental Methods

Improved methodology is required to improve our ability to identify products formed in precursor-product relationships. Specific methods which will be investigated include 1) liquid chromatography-mass spectrometry, 2) low level counting and, 3) high resolution capillary gas chromatography coupled to mass spectrometry.

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G. Flavor-Release Research

We will continue to pursue the synthesis of flavor-release compounds, with most of the activity

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being devoted to carbohydrate-based systems. In addition to the synthetic program, however, it is also planned to explore smoke chemistry problems using flavor-release compounds. Flavor-release compounds represent a unique opportunity to study smoke chemistry in that they are well characterized non-volatile compounds which give limited numbers of products on pyrolysis. In addition pyrolysis products are generally a function of temperature. Consequently, a detailed investigation of the behavior of flavor-release compounds on cigarettes should provide concrete information on the rates of heat transfer in a burning cigarette. As a consequence, not only does the area of flavor-release chemistry provide a potential source of new products, it also will greatly contribute to our understanding of smoke chemistry.

H. Selective Filtration of Flavorants

We are currently studying the transfer of tetramethylpyrazine to mainstream smoke using gas chromatographic techniques, and will shortly initiate a similar study with menthol utilizing radiochemical analytical techniques. Both of these compounds are of interest in that significant transfer from filler to filter takes place. As a consequence we will be able to determine the amount of flavorant transferring from the filter to mainstream smoke as well as the mechanism by which it transfers; e.g., vapor phase transfer, displacement, etc. This information may allow us to develop methodology for increasing the amount transferred from the filter which could result in more efficient utilization of certain flavorants.

I. Synthesis and Evaluation of New Flavorants

We will continue this ongoing project with most of the emphasis being placed on the synthesis of tobacco identical terpenoids.

J. Structure-Activity Relationship for Flavorants

This is a long-term project which has as its ultimate goal the development of an understanding

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of the relationship between a substance's structure and its flavor so that new flavorants can be prepared on a rational basis. The first stage of this program must be the establishment of non-subjective descriptors of flavor. We are presently investigating the use of multi-dimensional scaling techniques to accomplish this goal.

K. Nicotine Research

Our primary goals for this project continue to be the synthesis of a nicotine analogue which shows separation of effects and to elucidate the molecular mechanisms by which nicotine exerts its biological effects.

L. Service to Other Groups

A more detailed explanation of these programs is provided in the individual projects' plans and objectives which are attached.

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